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TITLE: Efficacy Study of a Fully Implanted Neuroprosthesis for Functional Benefit to Individuals with Tetraplegia

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

We propose to complete a Phase II Clinical Trial to demonstrate the safety and efficacy of a fully-implanted neuroprosthesis to provide upper extremity function for individuals with cervical SCI. This study will utilize the "networked neuroprosthesis" (NNP). The NNP system is completely implanted, including all power, signal processing, stimulus generation, and electrodes. We expect that this advanced system will lead to increased regular use of the neuroprosthesis, with a subsequent positive impact on quality of life. The completion of this study will allow us to proceed to broad dissemination of advanced neuroprosthetic systems for the provision of motor function in SCI and similar diseases.

15. SUBJECT TERMS

Nothing listed

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1. INTRODUCTION:

We propose to complete a Phase II Clinical Trial to demonstrate the safety and efficacy of a fully-implanted neuroprosthesis to provide upper extremity function for individuals with cervical SCI. We have completed a clinical feasibility study of a neuroprosthesis that provides myoelectrically-controlled hand grasp to this population. That device utilized external powering and processing, requiring the subjects to have assistance in donning and doffing the neuroprosthesis. We have now completed the design of a fully-implanted, modular neuroprosthetic system, the "networked neuroprosthesis" (NNP). The NNP system is completely implanted, including all power, signal processing, stimulus generation, and electrodes. This eliminates the requirement of having to wear any external components taped to the skin in order to gain hand function, which has been a requirement of all upper extremity neuroprostheses to date. We expect that these advances will lead to increased regular use of the neuroprosthesis, with a subsequent positive impact on quality of life. We have completed the development of this technology and have established a full supply chain for manufacture of this system. Recent funding from the State of Ohio has been obtained to develop this technology within the required manufacturing practices necessary for a commercial implantable medical device. In conjunction with the development of the technology, we have also developed and implemented a complete marketing strategy that is specifically targeted for implantable devices in SCI, with the NNP hand system as the first product. Thus, we are now fully equipped and prepared to conduct a Phase II clinical trial of this technology to demonstrate safety and efficacy. The completion of this study will allow us to proceed to broad dissemination of advanced neuroprosthetic systems for the provision of motor function in SCI and similar diseases.

2. KEYWORDS:

Neuroprosthesis
Functional Electrical Stimulation
Spinal Cord Injury
Paralysis
Rehabilitation
Upper Extremity
Implantable Medical Device
Tetraplegia

3. ACCOMPLISHMENTS:

What were the major goals of the project?

The major goal of the project was to **i**mplement the NNP System with 16 (ten supported by this proposal) cervical level spinal cord injured subjects and evaluate the resulting improvement in upper extremity function. Compare functional abilities with and without the use of the neuroprosthesis. The outcome assessments are designed around two hypotheses regarding the advantages of the NNP:

#1. We hypothesize that at least 70% of all subjects will demonstrate improved function compared to their baseline performance in one or more activities (primary outcome measure).

#2. We hypothesize that the proportion of subjects demonstrating daily usage (7 days/week) of the NNP System will be significantly higher than the published rate of daily usage for the first generation neuroprosthesis.

Project major tasks and milestones for the first 24 months of the project, showing percentage of completion as of 9/29/2016.

Major Task 1: Preparations and Support for Clinical Study	Months	% Completion	Notes
Subtask 1: Prepare Regulatory Documents and Research Protocol			
Coordinate Sites for IRB protocol submission at MHMC and LSVA	1	100%	
Submit screening protocol to IRB at MHMC and LSVA	2	100%	
Assemble response for IDE application to U.S. Food and Drug Administration (FDA)	1-5	100%	
Submit IDE response	5	100%	
Finalize consent form & human subjects protocol	5	100%	
Submit implantation protocol to IRB at MHMC and LSVA	5	100%	
Submit implantation protocol to HRPO	5	100%	
Assemble Clinical Events Committee	6	100%	
Submit amendments, adverse events and protocol deviations as needed	as needed		
Milestone Achieved: Local IRB approval of Screening Protocol at MHMC and LSVA	3	100%	
Milestone Achieved: IDE approval from FDA	7	100%	
Milestone Achieved: Local IRB approval at MHMC and LSVA	6	100%	
Milestone Achieved: HRPO approval for all protocols	7	100%	
Subtask 2: Acquire Networked Neuroprosthesis Systems (NNP)			
First round of purchases and assembly (3 systems)	6	100%	
Second round of purchases and assembly (3 systems)	12	50%	
Milestone Achieved: NNP Systems received and sterilized	7,13,17,21	33%	
Major Task 2: Conduct Clinical Study	Months	% Completion	Notes
Subtask1: Subject Screening			
Begin subject recruitment	6	100%	
Subject Screening	6-30	20%	
Milestone Achieved: 1st participant consented and screened	6	75%	
Milestone Achieved: Study begins	6	50%	
Subtask2: NNP Implantation			
Implant Subject #1	11	10%	[1]
Implant Subject #2	14	0%	
Implant Subject #3	17	0%	
Implant Subject #4	19	0%	
Implant Subject #5	21	0%	
Milestones Achieved: Subjects implanted	11-33	1%	
Subtask3: Subject Assessment			
Complete Outcomes Assessments with Subject #1	15	0%	
Complete Outcomes Assessments with Subject #2	19	0%	
Complete Outcomes Assessments with Subject #3	21	0%	
Complete Outcomes Assessments with Subject #4	23	0%	
Major Task 3: Data Analysis and Dissemination	Months		
Subtask 1: Data Analysis			
Perform all analyses according to specifications, share output and finding with all investigators	23-36	0%	
Milestone Achieved: IDE annual report submission	20,32	50%	
Subtask 2: Data Dissemination			
Presentation of results at national meetings	12-36	33%	
Preparation of manuscript #1 - first-in-man upper extremity NNP system case study	15	20%	
Milestone Achieved: Manuscript #1 submitted	18	0%	

Notes related to progress toward completion of project milestones:

[1] As described in the previous annual report, there were some significant initial hurdles in our project related to obtaining regulatory approval. These issues required some modification of the technology. However, we have completed all of those issues. We have performed the first human implant (under separate funding), but the results of this first implantation have a significantly positive impact on this project and moves us toward our goal of human implantation on this project. We are working hard now to begin the series of human implantation procedures under this grant.

What was accomplished under these goals?

The major accomplishment over the past year has been the first-in-man implantation of the Networked Neuroprosthesis (NNP) System in a spinal cord injured subject. Note that this subject was implanted under separate funding and is not part of the five subjects to be implanted in this study. However, the process of human implantation is critical to this SCIRP project, and is therefore briefly summarized here. Further, we identified an issue with respect to device heating that we have fully resolved this year, including obtaining a Supplement to our IDE.

The first human implantation of the NNP System was performed on January 12, 2016. The first subject was implanted with a system for grasp, reach, and postural stability. The NNP System included 20 stimulating electrodes, 4 myoelectric signal recording electrodes, 8 3-axis accelerometers, and 11 temperature sensors. All aspects of the system are functional and the subject is beginning exercise for muscle conditioning. An important aspect of the NNP design is the consideration for practical surgical implantation using standard surgical techniques. Figure 1A shows an x-ray of the complete system, showing the location of each of the modules. Modules are placed near the target muscles for stimulation and recording, and in locations that can be accessed for future surgical servicing (repair/replacement). Figure 1B shows an intraoperative picture of one of the stimulating leads being plugged into the stimulator module in the volar forearm.

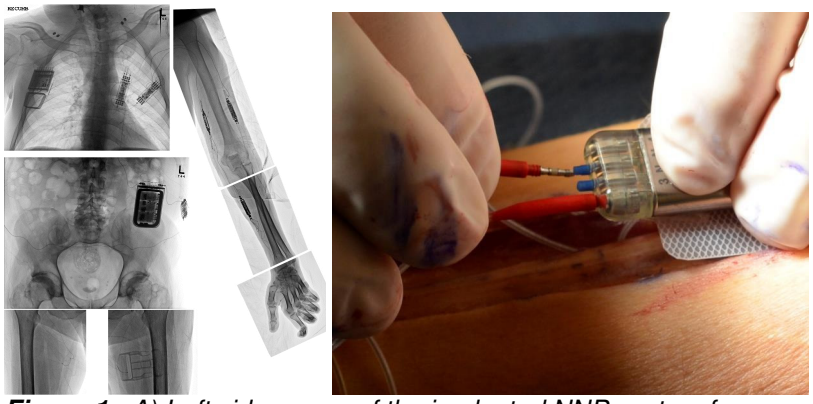

Figure 1. *A) Left side: x-ray of the implanted NNP system for grasp, reach, and postural stability. B) Right side: intraoperative picture showing color-coded connection of a stimulating electrode.*

The first subject has demonstrated functional independence ahead of schedule. Figure 2 shows the subject using the NNP hand grasp to hold a fork and stab a blueberry. The subject is unable to hold anything in his hand when the stimulation is off. He was also able to hold a pen and sign his name. Early testing with stimulation of the muscles in his trunk for postural stability (back extensors, hip extensors) demonstrated an increase of 8cm in sagittal reach when the stimulation was on compared to when the stimulation was off. Also, reach above the head and to the side is greatly improved with the addition of trunk stability.

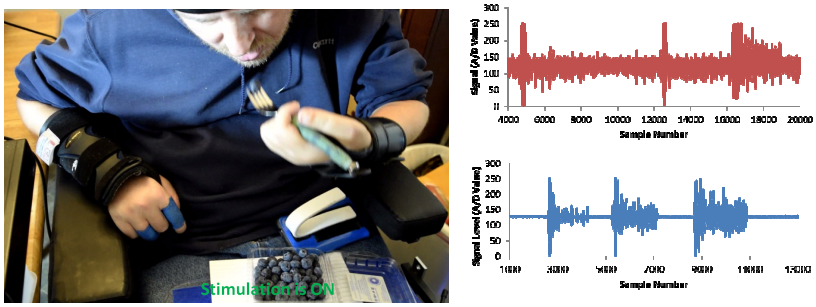

Figure 2. *Left: Subject using the NNP to grasp a fork and stab a blueberry. Right: Myoelectric signals recorded from the NNP during activation of the platysma muscle (top red) and trapezius muscle (bottom blue).*

With the first human implantation, we identified an issue with the heating of the power module inside the body, as well as heating of the recharge coil. The implanted power supply (the "Power Module") is designed to accommodate module heating during recharge and during functional operation off of the internal battery. Power Module temperature is monitored through four internal thermistors (a fairly unique feature of our system). Our early testing shows that the Power Module heats up faster than our bench testing predicted. This can be alleviated using a slower recharge rate, but this results in an excessive recharge time (15 or more hours to fully recharge the system). In initial testing with the subject post-implantation, we demonstrated that combining the recharge coil with an ice pack could potentially reduce the total recharge time to three hours or less. Given this promising observation, we proposed to design a water-cooled recharge coil that is practical for daily use by the subject.

We developed a water-cooled recharge coil and submitted the design to the FDA in a Supplement to our IDE. That Supplement was approved on May 19, 2016 and is in use with our first subject. The details of this new design are described in the following paragraphs.

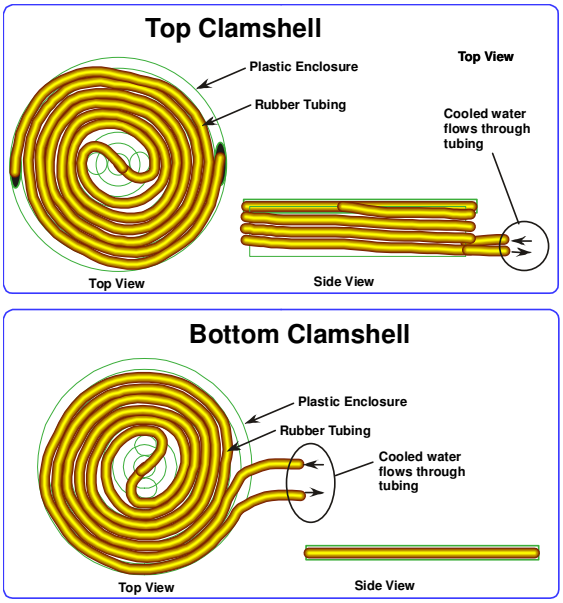

Figure 3. Descriptive figure of the Recharge Coil Enclosure.

Purpose of Coil design. The NNP Active Cooling Enclosure is a plastic, actively water-cooled enclosure for the NNP Recharge Coil. The active cooling maintains skin interface and implanted Power Module at or below the maximum temperature during recharge. The active cooling enclosure also completely encloses the external Recharge Coil so that the Recharge Coil itself does not touch the skin and cannot be touched or directly handled by the User.

Description of Coil Design. The External Recharge Coil was previously described in Section 2.6.1. It safely provides the appropriate time varying magnetic field required to recharge the Power Module. The External Recharge Coil was originally design to be applied directly on the skin over the site of the implanted Power Module. A thermistor is used to measure the temperature of the coil/skin interface. The 3.5 KHz drive level to the Recharge Coil is set in hardware such that the coil temperature at the coil/skin interface cannot exceed 41°C.

As part of the Early Feasibility IDE Study, we identified the External Recharge Coil and the recharging process as areas of examination with each subject to identify the most desirable and practical methods of recharge. Our first subject desires a rapid recharge time and is not concerned about the size of the external coil and enclosure. Therefore, we proposed an external enclosure that fits around the coil, provides active cooling, and protects against any direct contact with the coil. Using this enclosure, it is now possible to recharge the implanted NNP System in less than four hours, whereas the original design required approximately 14 hours.

Note that the enclosure fits around the existing External Recharge Coil. Therefore, there are **no design changes to the External Recharge Coil**, and it remains as previously described. The thermistor that measures the coil/skin interface temperature is placed on the lower (skin contact) surface of the enclosure rather than on the External Recharge Coil itself, as previously designed. This change is made because the important parameter is the temperature of the skin interface, not the temperature internal to the coil enclosure, which cannot be accessed by the User.

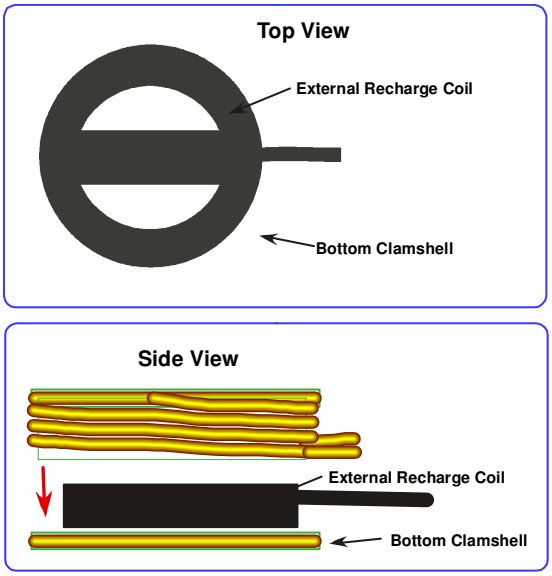

Figure 4. Enclosure placed around the External Recharge Coil.

The Recharge Coil Enclosure consists of two cylindrical clamshells, as shown in Figure 3 and Figure 4. The External Recharge Coil fits completely within the clamshells, with only a small opening for the coil cable to exit. The coil cable connects to the Control Tower, as previously described.

Each of the two clamshells is a hollow plastic (acetal, nylon, or polycarbonate) enclosure. Within the clamshell is wound a rubber tubing (Tygon A-60-F) as shown in Figure 3. Cooled water is pumped through the rubber tubing, providing a cooling effect to the skin and also cooling the external coil itself. Importantly, the cooling maintains the temperature of the outer surface of the Recharge Coil Enclosure below 41°C. The rubber tubing is completely enclosed within the plastic clamshells.

The two halves of the Recharge Coil Enclosure are connected together around the External Recharge Coil and completely enclosed with polyethelyne adhesive tape. The thermistor is placed on the bottom surface of the enclosure, which is in direct contact with the skin. Therefore the thermistor measures the temperature of the skin/enclosure interface.

The clamshell is cooled using two Peltier-based cooling pumps (003-07 ThermaZone™ Continuous Thermal Therapy Device). Each pump has a maximum cooling of 4°C and uses distilled water to pump through the tubing within the Recharge Coil Enclosure. The pumps are turned on by the User prior to placing the coil enclosure over the skin. As our testing shows, the cooling effect of these devices while the coil is recharging is typically in the range of 19-23°C (i.e. typically slightly below room temperature).

Results. The Recharge Coil Enclosure was utilized to fully recharge the NNP System in the first subject while in the lab under constant monitoring. The results are shown in Figure 5. The maximum PM temperature was 39.7°C, corresponding to a PM/tissue temperature of 38.7°C. The water-cooled enclosure has the effect of cooling the tissue down to the depth of the PM, as indicated by the steady decrease in PM temperature after ~40 minutes of recharge. The temperature of the skin/enclosure interface was maintained at 19-22°C. This temperature steadily decreased during the 150 recharge period, demonstrating that the cooling pumps are more effective over time. This data was obtained with a 50mA recharge rate per battery, which corresponds to a full recharge from a full discharge in a 3.5 hour period. This allows the subject to recharge in the morning or evenings when he has an aide available to help with positioning of the external coil.

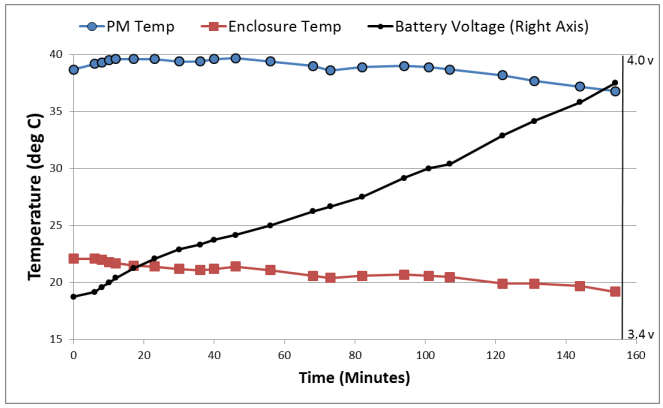

Figure 5. Results of the water-cooled recharge coil compared to the original coil design.

What opportunities for training and professional development has the project provided?
"Nothing to Report."

How were the results disseminated to communities of interest?
"Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.
We are ready to begin implantation of NNP systems in human subjects, now that we have obtained OHRP approval. We do have a yield issue with respect to the fabrication of the remote modules (stimulators, biopotential recording) for the NNP. As a result, it may require more time to fabricate a complete set for implantation, but we will be able to achieve this successfully. Once the first subject has been implanted, the study protocol will be followed, including muscle conditioning, system programming, functional training and outcomes assessment. See Section 5. **Actual or anticipated problems or delays and actions or plans to resolve them** for additional details.

4. IMPACT:

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What was the impact on the development of the principal discipline(s) of the project?

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project.
We have demonstrated the power of a modular implantable system. Besides the obvious benefits of configurability with respect to multiple clinical applications, we have demonstrated the power of the modular approach to be resistant to component failures. Specifically, the modular approach provides significant functional redundancy.

What was the impact on other disciplines?
Nothing to report.

What was the impact on technology transfer?
Nothing to report.

What was the impact on society beyond science and technology?
Nothing to report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change
Our approach remains the same. However, we have identified yield issues in the fabrication of the remote modules. This requires additional testing of each unit and may require us to fabricate a higher number of components in order to achieve the total number required for each human implantation.

Actual or anticipated problems or delays and actions or plans to resolve them
We have resolved all of the initial design issues described in the first year report. We now have a working system in our first human subject for a period of nine months of follow-up. This indicates the durability of the technology and positions us for additional surgical procedures. However, the issues of initial design refinements, and issues of manufacturing yield, have resulted in a delay in the initiation of the implantation of subjects for this project. Having successfully achieved the first human implantation, however, is a very significant milestone. We have now achieved full approval from the FDA, from our local IRB, and from HRPO. We will now work to efficiently proceed with implantation procedures as we go forward in this project. Our specific strategy for beginning human implantation on this project and meeting the original goals of this SCIRP study are outlined in the paragraphs that follow, and include the following key aspects: 1) recruitment, 2) scheduling logistics, 3) surgical planning, 4) overall study timeline, 5) study goals, and 6) importance of subject follow-up to SCIRP study goals.

It should be noted that the project we are proposing is a significant undertaking. We are seeking to achieve functional improvements in severely paralyzed individuals – patients who do not have any other treatment options. For the past 70+ years, treatment for SCI has been fundamentally the same, without significant improvements in independence. Our technology, utilizing the NNP System, is the first to achieve a step increase in independence. Further, we are also groundbreaking with respect to our regulatory process. We were one of nine teams around the country who were selected into the Pilot Early Feasibility Program at the FDA. We have also recently been selected to be a part of the Expedited Access Program at the FDA, and *it is likely that we are the only team in the entire country to have been selected to participate in both of those programs.* We are seeking to propel the world's first modular, fully-implantable, and operational motor neuroprosthesis through a human trial. This is a difficult endeavor, but one we are capable of completing. However, it is certainly difficult to predict in advance the duration of each new roadblock we encounter since there are no similar predicates on which to base our projections. *We do expect to complete the project as proposed*, but we acknowledge that we are almost certainly unlikely to complete the project within the originally proposed timeframe (see point #4 below). Despite this, the outcome with respect to the proposed tasks will be completed and, we are confident, will be completed successfully, demonstrating the desired outcome of significantly increased independence and utility of implanted neuroprostheses for cervical SCI.

Our specific mitigation strategy is as follows:

1) Recruitment. We do not anticipate any problems with subject recruitment. Over the past decade we have typically averaged about 50 patient referrals per year and we currently have a waiting list of over 200 patients who are interested in participating in our research. We currently have eight subjects who have been screened in the past and who have expressed interest in obtained the NNP implanted system. All of these subjects are excellent candidates, and two have already been fully consented for the NNP implantation procedure. We do not routinely proceed with full consent for all subjects screened until we are closer to the actual implantation surgery for each subject. In addition to the eight candidates who are ready, we screened an addition five subjects in the past year, all of whom are potential candidates. Thus, we have 13 subjects screened, which should be more than sufficient for the completion of the SCIRP study. We will, however, continue to screen interested subjects who contact our research team seeking involvement in our research.

2) Scheduling Logistics. We do anticipate that the logistics of scheduling subjects will be a difficulty as we proceed forward. Specifically, our experience has been that SCI subjects frequently encounter various health and life challenges, such as the development of a pressure sore, urinary tract infection, pneumonia, or even the loss of a reliable attendant for a period of time. These issues present a challenge when scheduling implantation surgeries, particularly when the scheduling process also involves the surgical and research team schedules. It is to be expected that there will be, on occasion, delays in a surgical procedure due to health concerns and that some procedures will be postponed from their originally planned date. A key mitigating milestone in addressing scheduling logistics is that *we are completing the construction of a first-of-its-kind long-term stay facility for our research subjects* that is adjacent to our rehabilitation hospital and to our research laboratories. This facility essentially serves as a hotel for longer (weeks to months) patient stays. Among the features of this facility is that it is designed specifically for individuals with cervical SCI, and includes fully accessible bedrooms, bathrooms, and kitchen; as well as motorized ceiling-mounted patient lifts, roll-in showers, and separate caregiver rooms. *This facility is scheduled to open May 2017* and will provide us with a significant increase in our flexibility with respect to recruitment. Specifically, among other advantages, subjects can re-locate to Cleveland for the period of the study. We have already had a number of subjects express interest in this alternative, and our first subject for our SCIRP project is relocating to Cleveland from Miami for a period of three months in order to participate in the study. Thus, the opening of this facility will allow us to recruit nationally and will significantly reduce the logistical difficulties that we usually encounter when recruiting long-distance subjects.

3) Surgical Planning. We will have to use an exponential implantation strategy to catch up with the originally proposed plan as outlined in our SOW. We have done this in the past and, in fact, this is typical of the uptake of implanted neuromodulation devices [e.g. cochlear implants, bladder implants, hand neuroprosthesis]. This approach maximizes the learning we can gain from the first few patients, but also maximizes the overall uptake. The specific rate of update will be divided into four four-month (1/3rd year) periods over the last 16 months of the granting period:

Period 1 – 1 subject
Period 2 – 2 subjects
Period 3 – 3 subjects
Period 4 – 4 subjects
Total – 10 subjects

We have achieved this rate of uptake in the past and, in fact, have exceeded this rate (i.e. we implanted 12 subjects in 13 months) with our previous generation neuroprosthesis. Thus, we understand the infrastructure and preparations that are necessary to achieve this ambitious rate and we are confident we can achieve these projections.

4) Overall Study Timeline. In order to achieve the total subject uptake as outlined below, we anticipate requesting a no-cost extension to the current grant period. Specifically, this would extend the grant period to 9/31/2018. This would provide us with sufficient time over which to schedule surgical procedures and to accommodate the occasional postponement of a surgical procedure. We are currently establishing the infrastructure that will allow us to do this, including building the implantable component inventory and establishing the patient housing, as described above. We are currently working with our manufacturing partners to ensure that we will be able to obtain the hardware and related components for the complete cohort.

5) Focus on Study Goals. It is important to note that the study goal is to demonstrate the outcome measures we propose and to achieve our Specific Aims, specifically *demonstrating statistical significance for our two study hypotheses*. We will perform an interim analysis to determine a more precise sample size requirement for each hypothesis. Further, we are already able to begin collecting data with regarding to home usage of the NNP system and we will have our first report on these results in QPR#2 for Year 3. This data will directly supplement our study analysis and directly contributes to the statistical analysis performed for hypothesis #2 (regular device usage) for our SCIRP project.

6) Importance of Subject Follow-up to SCIRP Study Goals. It should be noted that although the first-in-human subject (and additional subjects to be reported in the QPRs for Year 3) was not implanted directly as part of SCIRP funding, this subject will be followed under the SCIRP proposal to gain information on device usage rates and technology reliability. Thus the SCIRP study greatly benefits from this additional information and, in fact, cannot be completed without it. We will continue to report on these implantation procedures to keep the CDMRP updated with respect to the ongoing results from these subjects.

Changes that had a significant impact on expenditures
Despite the difficulties in the design refinements and manufacturing yield, we still are on track to be able to complete the originally targeted subject population within budget.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Nothing to report.

6. PRODUCTS:

Publications, conference papers, and presentations
Kilgore KL, "New Concepts in Networked Implantable Systems"; Neuromodulation: The Science Conference, San Francisco, CA, May, 2016.
Kilgore KL, Bryden AM, Peckham PH, Keith MW, Triolo RJ, DiMarco A, Gustafson KJ, Hoyen HA, Nemunaitis G. Advanced Implantable Neuromodulation Systems. International Microwave Symposium, San Francisco, CA, May 22-26, 2016.
Kilgore KL, Hoyen HA, Keith MW, Triolo RJ, Bryden AM, Lombardo L, Hart RL, Miller M, Nemunaitis GA, Peckham PH. "Implanted network for motor function in cervical SCI", ASIA 2016 Annual Meeting, Philadelphia PA, April, 2016.

Website(s) or other Internet site(s)
http://restorefunction.org/

Technologies or techniques
Nothing to report.

Inventions, patent applications, and/or licenses
Nothing to report

Other Products
Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
PI: P. Hunter Peckham
Others:
Anne Bryden
Brian Smith
Kevin Kilgore
Megan Moynahan
Michael Keith
Harry Hoyen
Greg Nemunaitis
Ron Hart
Antonia Wilson
Alex Campean
Betty Dunger

Provide the name and identify the role the person played in the project.
If information is unchanged from a previous submission, provide the name only and indicate "no change".

Name: Hunter Peckham
No change in role, person months, or contribution from the original submission.

Name: Anne Bryden
No change in role, person months, or contribution from the original submission.

Name: Brian Smith
No change in role, person months, or contribution from the original submission.

Name: Kevin Kilgore
No change in role, person months, or contribution from the original submission.

Name: Megan Moynahan
No change in role, person months, or contribution from the original submission.

Name: Michael Keith
No change in role, person months, or contribution from the original submission.

Name: Harry Hoyen
No change in role, person months, or contribution from the original submission.

Name: Greg Nemunaitis
No change in role, person months, or contribution from the original submission.

Name: Betty Dunger
No change in role, person months, or contribution from the original submission.

Name: Antonia Wilson
No change in role, person months, or contribution from the original submission.

Name: Ron Hart
No change in role, person months, or contribution from the original submission.

Name: Mary Ann Richmond
No change in role, person months, or contribution from the original submission.

Name: Alex Campean
No change in role, person months, or contribution from the original submission.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

P. Hunter Peckham
Nothing to report.

Kevin L. Kilgore
Two new grants started in the past year:

Grants started during this reporting period:

Title:	"Phase 2 Study of a Networked Neuroprosthesis for Grasp, Reach, and Trunk Function in Cervical Spinal Cord Injury" R01-FD-005409
Commitment:	1.13 Calendar-months
Funding Agency:	FDA Orphan Products Division
Grants Officer:	Christine Mueller
Performance Period:	9/15/2016-8/31/2020
Funding Level:	$338,451
Goals:	The goal of this study is to implement and implant a networked neuroprosthesis in cervical spinal cord injury to provide grasp, reach, and trunk function.
Specific Aims:	The Specific Aim of this study is to demonstrate the safety and efficacy of the NNP Grasp and Trunk System. This will be accomplished in four stages: 1. Finalize the technology features that allow convenient home use and assessment of daily usage rates. 2. Implant six subjects with the NNP Grasp and Trunk System. 3. Perform training and assessments on these subjects in functional activities related to grasping, reaching, and trunk movements. 4. Assess daily usage of the neuroprosthesis at home and in the community in all eleven subjects.
Overlap:	No scientific overlap exists between this grant and the proposed project. These are separate subjects and will receive a multi-function system.

Title:	"Investigation of Charge Balanced Direct Current Block"
Commitment:	0.44 calendar-months
Funding Agency:	Halyard Health Sponsored Research Agreement
Grants Officer:	Phil Schorr
Performance Period:	6/30/2016-12/29/2017
Funding Level:	$275,000

Goals:	The purpose of this project is to evaluate the use of charge-balanced direct current block to alleviate chronic and acute pain.
Specific Aims:	Acute studies to evaluate charge-balanced electrical nerve block.
Overlap:	No scientific overlap exists between this grant and the proposed project.

Michael W. Keith
Nothing to report.

Harry A. Hoyen
Nothing to report.

Greg Nemunaitis
Nothing to report.

Mary Ann Richmond
Nothing to report.

Megan Moynahan
Nothing to report.

Anne Marie Bryden
One grant started during the past year.

Title:	"Phase 2 Study of a Networked Neuroprosthesis for Grasp, Reach, and Trunk Function in Cervical Spinal Cord Injury" R01-FD-005409
Commitment:	3.0 Calendar-months
Funding Agency:	FDA Orphan Products Division
Grants Officer:	Christine Mueller
Performance Period:	9/15/2016-8/31/2020
Funding Level:	$338,451
Goals:	The goal of this study is to implement and implant a networked neuroprosthesis in cervical spinal cord injury to provide grasp, reach, and trunk function.
Specific Aims:	The Specific Aim of this study is to demonstrate the safety and efficacy of the NNP Grasp and Trunk System. This will be accomplished in four stages: 1. Finalize the technology features that allow convenient home use and assessment of daily usage rates. 2. Implant six subjects with the NNP Grasp and Trunk System. 3. Perform training and assessments on these subjects in functional activities related to grasping, reaching, and trunk movements. 4. Assess daily usage of the neuroprosthesis at home and in the community in all eleven subjects.
Overlap:	No scientific overlap exists between this grant and the proposed project. These are separate subjects and will receive a multi-function system.

What other organizations were involved as partners?
Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS:
QUAD CHART: In appendix.

Efficacy Study of a Fully Implanted Neuroprosthesis for Functional Benefit to Individuals with Tetraplegia

SC130252
W81XWH-14-2-0173

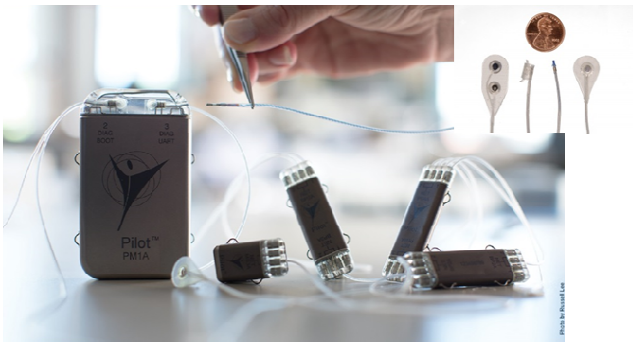
PI: P. Hunter Peckham **Org:** Case Western Reserve University, Cleveland, OH **Award Amount:** $2,363,423

Study/Product Aim(s)

•Task #1 – Implement ten cervical level spinal cord injured subjects and evaluate the resulting improvement in upper extremity function. Compare functional abilities with and without the use of the neuroprosthesis.

Approach

The outcome assessments are designed around two hypotheses regarding the advantages of the Networked Neuroprosthesis (NNP): #1. We hypothesize that at least 70% of all subjects will demonstrate improved function compared to their baseline performance in one or more; and #2. We hypothesize that the proportion of subjects demonstrating daily usage of the NNP System will be significantly higher than the published rate of daily usage for the first generation neuroprosthesis.



Accomplishment: Regulatory approval obtained from FDA; IRB approval nearing completion. First systems acquired (as shown above). All received systems have been fully tested and have been sent for sterilization. Additional acquisitions in Q1, Y2.

Timeline and Cost

Activities PY	1	2	3	
Regulatory and Administrative				
Technology Acquisition				
Implantation of NNP				
Assessment of Outcomes				
Estimated Budget ($K)	$792	$446	$262	$000

Updated: Oct. 30, 2016

Goals/Milestones (Example)

PY1 Goal – Complete Regulatory; Acquire first systems, First implant
☑ IDE
☑ Acquire first systems (100% complete)

PY2 Goals – System Implantation and Evaluation
☐Acquire technology (30% complete)
☐System Implantation (10% complete)
☐System Evaluation – Functional Assessments

PY3 Goal – System Implantation and Evaluation
☐ System Implantation
☐ System Evaluation – Functional Assessments

Comments/Challenges/Issues/Concerns

- All regulatory approvals obtained. Design refinements completed. Encountered manufacturing yield issues.
- Delay in first surgery – still expect to complete project in 3 years.

Budget Expenditure to Date

Projected Expenditure: $1.23M
Actual Expenditure: $900K (delay in system acquisition)